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Application No: 09/874,091

Re: 1. Transmittal of Reply Brief in Response to Examiner's Answer  
2. Reply Brief to Examiner's Answer

Pages Including Cover Sheet(s): 11

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: Charych, et al.

Attorney Docket No.:  
1680.002/CHIRP014

Application No.: 09/874,091

Examiner: Tran, My Chau T.

Filed: June 4, 2001

Group: 1639

Title: MICROARRAYS FOR PERFORMING  
PROTEOMIC ANALYSES**CERTIFICATE OF FACSIMILE TRANSMISSION**I hereby certify that this correspondence is being transmitted by  
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Signed: \_\_\_\_\_

Tara Hayden

**TRANSMITTAL OF REPLY BRIEF  
IN RESPONSE TO EXAMINER'S ANSWER**Mail Stop Appeal Brief-Patents  
Commissioner of Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Transmitted herewith in triplicate is the Reply Brief In Response To Examiner's  
Answer mailed November 27, 2006.This reply brief is being filed within two (2) months of the mailing date of the  
Examiner's Answer.Applicant believes that no extension of term is required. If an additional extension of  
time is required, however, please consider this a petition therefor.☒ Charge any additional fees or credit any overpayment to Deposit Account No.  
500388, (Order No. CHIRP014).Respectfully submitted,  
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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EX PARTE Charych *et al.*

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Application for Patent

Filed: June 4, 2001

Serial No. 09/874,091

Examiner: My Chau T Tran

Art Unit: 1639

FOR:  
MICROARRAYS FOR PERFORMING PROTEOMIC ANALYSES

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REPLY BRIEF TO EXAMINER'S ANSWER

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**(1) STATUS OF CLAIMS**

There are a total of 33 claims pending in this application (claims 1, 60-73 and 79-91 and 97-101). Claims 2-59, 74-78 and 82-96 have been cancelled. Claims 1, 60-73, 79-91 and 97-101 have been examined and rejected.

Specifically, claims 1, 60, 61, 63-66, 73, 79, 80, 82-85, 97, 98 and 99-101 are rejected under 35 U.S.C. §103(a) as being unpatentable over US Patent No. 5,478,527 to Gustafson et al. ("Gustafson") in view of US Patent No. 6,087,102 to Chenchik et al. ("Chenchik").

Claims 62 and 81 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gustafson and Chenchik, as applied above to claim 1 or 73, and further in view of US Patent No. 6,329,209 to Wagner et al. ("Wagner").

Claims 67-72 and 86-91 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gustafson and Chenchik, as applied above to claim 1 or 73, and further in view of US Patent No. 5,482,867 to Barrett et al. ("Barrett").

The rejection of each of claims all claims under § 103 is appealed.

**(2) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL**

Claims 1, 60-73 and 79-91 and 97-101 are pending in the application.

Claims 1, 60, 61, 63-66, 73, 79, 80, 82-85, 97, 98 and 99-101 stand rejected under 35 U.S.C. §103(a) as being unpatentable over US Patent No. 5,478,527 to Gustafson et al. ("Gustafson") in view of US Patent No. 6,087,102 to Chenchik et al. ("Chenchik").

Claims 62 and 82 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Gustafson and Chenchik, as applied to claim 1, and further in view of US Patent No. 6,329,209 to Wagner et al. ("Wagner").

Claims 67-72 and 86-91 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gustafson and Chenchik, as applied to claim 1, and further in view of US Patent No. 5,482,867 to Barrett et al. ("Barrett").

**(3) ARGUMENTS**

The arguments in this Reply Brief address the specific contentions raised in the Examiner's Answer of November 27, 2006.

Much of the difference between the Appellants' and the Examiner's positions is whether the diffraction gratings of Gustafson are relevant to protein arrays in general, and specifically to the protein arrays of Chenchik. Appellants have repeatedly argued that these references teach disparate types of assays that differ greatly in both function and structure. These fundamental differences between the assays and associated products of Gustafson and Chenchik include:

1) Physical principle on which the assays are based on: Diffraction or disturbance of incident light on the biograting to produce a diffraction pattern indicating the presence of a single analyte (Gustafson) vs. emission of different signals from multiple probes, each signal indicating the presence of the binding partner of the associated probe (Chenchik);

2) Arrangement: Densely bound parallel lines (or linear zones) of a single type of binding reagent (Gustafson) vs. multiple discrete patches of labeled probes (Chenchik); and

3) Single binding partner of analyte (Gustafson) vs. multiple binding partners (Chenchik).

As discussed in Amendments and the Appeal Brief, the assays described by Gustafson and Chenchik differ significantly in structure and function and are based on entirely different physical principles. Because of these differences, one of skill in the art would not have viewed the biogratings of Gustafson as relevant to protein arrays and would not have been motivated to combine the references. Even if one were to combine the references, there is no teaching or suggestion of how to combine the references to make the "hybrid" diffraction-grating/protein array assay that the Examiner suggests. Appellants are unaware of such an assay, and the Examiner has not provided any explanation of how the references might be combined to produce such an assay.

In the Examiner's Answer, the Examiner attempts to address Appellants' arguments, but still has not provided any reasonable motivation to combine these very disparate references, nor any explanation of how such a combination would be operable. Appellants address each of the Examiner's specific contentions found on pages 24-27 of the Examiner's Answer below. (The remainder of the Answer duplicates the Examiner's arguments found in previous Office Action and addressed in Appellants' Appeal Brief; or duplicates the below-addressed arguments with regard to other claims). First, the

Examiner contends that Appellants misinterpret Gustafson and Chenchik in describing the very different structures:

It is the examiner's position that appellant misinterprets figures 1 and 4 of Gustafson in that the *only* arrangement of the targets are parallel lines...As clearly stated in Gustafson et al., figures 1 and 4 are illustrations of the *cross-sectional view* of an embodiment of the invention...These illustrations provide two possible interpretations of the arrangement of the targets that are parallel lines as interpreted by the Appellant *and* linear zones as depicted by figure 1 of Chenchik et al...Consequently the structural features of the product are not different. (Examiner's Answer, item (A)(1), pages 24 and 25).

Appellants respectfully submit that the Examiner misinterprets both Gustafson and Chenchik. Appellants' illustration of Gustafson unambiguously shows the top view of Figure 1 in Gustafson. There is no doubt from the discussion of Figure 1 in Gustafson, as well as a basic understanding of diffraction gratings, that assay of Gustafson requires linear zones or parallel lines of active and non-active binding reagent. Diffraction gratings by definition are spaced parallel lines that diffract incident light into specific angles as contrasted to being scattered in all directions. If the Examiner aware of a diffraction grating that does not require parallel lines or linear zones, Appellants respectfully submit that the Examiner supply such a reference. There is certainly no teaching or suggestion in any of the cited references that one may form a diffraction grating in another fashion. (Appellants are also unsure of the distinction the Examiner is making between "parallel lines" and "linear zones" in Gustafson - Gustafson clearly shows linear zones of active/non-active binding reagent forming parallel lines).

This distinction is important because the assays of Chenchik rely on discrete patches, each of a different analyte. Appellants reiterate their point that contrary to the Examiner's contention, Chenchik does not show linear zones of a single analyte (as in Gustafson) but multiple discrete patches (in Figure 1 arranged in a grid), each patch different analyte. Although these patches or spots may be arranged in lines, each spot is a binding partner corresponding to a different analyte, ordered by size. This is consistent with a basic understanding of assays employing labeled probes, in which the pattern of probes is largely immaterial. See, e.g., col. 5, lines 35-38 of Chenchik. ("The pattern of targets may take on a variety of configurations as long as each position in the array represents a unique size.") In use, if an analyte solution contains the binding partner of the biograting target in Gustafson, dense parallel lines are formed making a diffraction

grating. By contrast, in use, only isolated patches of the grid Chenchik corresponding to analytes present in the analyte solution (e.g, only A and D in the annotated drawing on page 10 of Appellants' Reply Brief) are bound and emit signals. Thus, contrary to the Examiner's contention, the structural features of the respective products of Gustafson and Chenchik are very different.

Next the Examiner contends that Gustafson somehow suggests an assay that employs labeled probes:

*"Although Gustafson et al.[s] preferred embodiment if for label-free assay, it is the Examiner's position that Gustafson et al. do suggest using label assay. Gustafson et al. define the term "diffraction grating" "to include gratings which are formed in one or more immunological steps. For the method of this invention, the diffraction grating is formed directly by conjugation of the non-light disturbing binding reagent on the insoluble surface with a light disturbing analyte" (see e.g. col. 4, lines 41-58), and the term "light disturbing" "to include all ways in which light is affected including light absorbing, reflecting, scattering, refracting and phase changing. From these definitions, the binding of the reagent and analyte would produce a detectable pattern on the surface wherein the analyte would include a label analyte. Accordingly, Gustafson et al. do suggest using a label assay." (Examiner's Answer, item (A)(2), pages 25 and 26).*

Appellants respectfully disagree and submit that nothing in the above-cited passages of Gustafson suggest labeled probes. Appellants again note that labeled probes are no more or less "light disturbing" than unlabeled probes, or any other molecule for that matter. Appellants submit that the Examiner is missing a fundamental difference between protein array assays (as in Chenchik) and diffraction gratings. Diffraction gratings disturb incident light. Labeled probe arrays, by contrast, do not require or use incident light, but work by emitting fluorescent or other signals when an individual probe is bound. Such probes do not disturb incident light in any particular manner that is at all relevant to a grating as discussed in Gustafson. Specifically labeled probes are not used in the assays of Chenchik to "absorb, reflect, scatter, refract or phase change" incident light. Each individual probe may be bound or unbound, the emitted signal from bound probes indicating the presence of the binding partner in the analyte solution. The bound probes do not disturb or affect light in any way meaningful to the assay, rather they emit it.

The Examiner contends that Chenchik suggests forming a diffraction pattern. Specifically the Examiner states (italics quoting from Appellants' Appeal Brief):



First, figure 1 of Chenchik et al. illustrate a pattern arrangement of the target on the surface of a solid support, i.e., '*a diffraction grating may be formed by any arrangement of its patches*,' (see fig. 1; col. 5, lines 64-67.) (Examiner's Answer, item A(3), page 26)

Appellants note that the italicized passage above is not quoted from the cited portion of Chenchik (as it may appear) but from page 11 Appellant's Appeal Brief discussing how Chenchik does not teach or suggest a diffraction grating. Appellants submit that the actual cited passage of Chenchik in no way teaches or suggests that a diffraction grating may be formed. Specifically, col. 5, lines 64-67 of Chenchik state the following "In FIG. 1, array 10 consists of a solid support 16 on the surface of which is presented a polymeric targets arranged according to size." Appellants submit that there is no reasonable interpretation of this or anything in Chenchik of the support shown in Figure 1 to be a diffraction grating. The Examiner appears to be taking a position that literally any arrangement of targets bound to a surface forms a diffraction grating. This position is incorrect. As is explained in Gustafson, and is generally known, diffraction gratings are formed by parallel lines that diffract light in characteristic ways. This is nowhere disclosed in Chenchik – Appellant's note that even if the multiple discrete patches of differently labeled probes in Chenchik were dense enough to form parallel lines required for a diffraction grating (and there is no teaching that they are), in use only the scattered isolated patches corresponding to the analytes present in the analyte solution are bound. These scattered patches would not form a diffraction grating.

The Examiner then states with regard to Chenchik:

Second, Chenchik et al. disclose that after the binding of the probe and target the hybridization patterns of the labeled probed can be visualized and detected, i.e., '*diffraction patterns may be used to detect the presence of proteins in the sample solution*,' (see col. 10, lines 38-45). (Examiner's Answer, item A(3), page 26, italics quoting from Appellants' Appeal Brief)

Again, Appellants note that the italicized passage is not quoted from Chenchik (as it may appear) but from Appellants' discussion of the Chenchik reference in the Appeal Brief. The cited passage of Chenchik discusses various methods by which labeled probes may be detected, including by scintillation counting, autoradiography, fluorescence measurement, calorimetric measurement, light emission measurement and

the like. All of these methods are known and appropriate methods of measuring differential expressions of labeled probes in an array – detection of bound proteins by emission of fluorescent or other light, heat, etc. What they do not teach or suggest is that a grid or array of different binding partners may somehow also be used to form a diffraction pattern or that light incident on such an array would give any meaningful pattern. This distinction is important because, as discussed in Appellants' Appeal Brief, the substrate of Gustafson would have been viewed as being particular to its own type of assay, which is fundamentally different from the protein arrays discussed in Chenchik.

With regard to Appellants' arguments that introducing multiple binding reagents or targets to the substrates of Gustafson would render the diffraction gratings unsuitable for their intended purpose, the Examiner contends that the teachings of Gustafson and Chenchik are analogous because both relate to binding probes and targets to produce detectable patterns on the surface of the support. (Examiner's Answer, item B, pages 26 and 27).

First, Appellants submit that while Gustafson is premised on detecting a diffraction pattern, the assays of Chenchik are not concerned with the resulting pattern, but whether there is a signal detected for the binding target corresponding to a particular analyte of a particular size.

Second, Appellants' argument is that because the biogratings of Gustafson are premised on a single target bound on a substrate densely enough to form parallel lines that will diffract incident light when bound to its analyte partner, the Examiner's proposed modification to include a plurality of protein binding agents would no longer function as a diffraction grating (picture for example, only two or ten bound targets of a one hundred target protein array – this arrangement of bound targets would not produce a diffraction pattern). Nothing in the Examiner's Answer explains how one might modify Gustafson to include a plurality of protein binding agents to produce a workable diffraction grating assay.

The Examiner also points to col. 4, lines 56-67 of Chenchik as supplying a motivation which discuss to use silicon dioxide. Appellants note that contrary to the Examiner's contention, silicon dioxide is not a metal oxide.

Finally, with regard to the Examiner's remarks regarding the Declaration of Deborah Charych (Examiner's Answer, item C, page 27), Appellants reiterate that they are relying on the Sections 1-4 and 6 of the Declaration – i.e., the portions of the

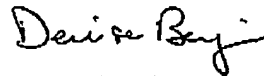
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regarding how one of skill in the art would interpret Gustafson and its relevance to the present invention. Accordingly, Appellants submit that the Examiner's comments regarding the thickness of the silicon dioxide layer are not relevant to the portions of the Declaration relied on by Appellants. Appellants submit that the relied upon sections meet the requirements MPEP 716.01(c)(III) and are entitled to consideration as relevant to how one of skill in the art would interpret and view the Gustafson reference.

### Conclusion

In view of the foregoing, it is respectfully submitted that none of the pending claims are rendered unpatentable by the cited references. Accordingly, the pending rejections of all of the claims under 35 U.S.C. § 103 should be reversed.

Respectfully submitted,  
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